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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,687	10/12/2001	Maureen R. Hanson	019603-002861	1127
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NIXON PEABODY LLP ATTENTION: DAVID RESNICK 101 FEDERAL STREET BOSTON, MA 02110				
EXAMINER LAMBERTSON, DAVID A				
ART UNIT		PAPER NUMBER		
1636				

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

844

Office Action Summary

Application No.

09/976,687

Applicant(s)

HANSON ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,11-16,18, 20 and 22-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,11-16,18,20 and 22-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed September 29, 2003. Amendments were made to the claims.

Claims 1, 3-6, 11-16, 18, 20 and 22-41 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed March 26, 2003, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action or sets forth rejections necessitated by amendment to the claims, this Office Action is made FINAL.

Information Disclosure Statement

The information disclosure statement filed August 8, 2003 has been considered, and a signed and initialed copy of the form PTO-1449 has been attached to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 38 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is necessitated by amendment.**

Claim 25 is dependent on claim 21, which is cancelled in the instant amendment.

Because claim 21 is cancelled, it is unclear what limitations apply to claim 25.

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Claims 38 and 39 recite the limitation "the non-plant eukaryotic host cell" in the first line of the claims. There is insufficient antecedent basis for this limitation because claim 34, from which each claim depends (as made by amendment), fails to mention that the "non-plant host cell" is a eukaryotic host cell.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-6, 11-16, 18, 20 and 22-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamilton 1997 in view of Hamilton '744, de Groot et al. (as cited in the previous Office Action) and Bundock et al. (as cited in the previous Office Action). **This rejection is both maintained for reasons as set forth in the previous Office Action and necessitated by amendment of the claims to include the limitation "wherein said non-plant host cell is a yeast cell, filamentous fungi or mammalian cell."**

Response to Arguments Concerning Claim Rejections - 35 USC § 103

Applicant's arguments filed September 29, 2003 have been fully considered but they are not persuasive. Applicant's arguments as they concern the rejection of claims 1, 5-6, 11, 13-16, 18, 20, 22-29, 31, 34 and 39 over Hamilton 1997 in view of Hamilton '744 are moot in view of

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the rejection of these claims over Hamilton 1997 in view of Hamilton '744, de Groot and Bundock. However, the arguments are implicitly discussed below.

Applicant's arguments filed September 29, 2003 have been fully considered but they are not persuasive. Applicant's arguments as they concern the rejection of claims 1, 3-6, 11-15, 18, 20, 22-30, 32-38, 40 and 41 over Hamilton 1997 in view of Hamilton '744, de Groot and Bundock consist of the following points:

1. The secondary references (Hamilton '744, de Groot and Bundock) do not make up for the deficiencies in the primary reference (Hamilton 1977), which does not teach a method of introducing a heterologous DNA into a non-plant host cell that is a yeast cell, filamentous fungi cell, *S. cerevisiae*, *K. lactis*, or *Aspergillus* (see for example the 7th and 8th paragraphs of page 12 of Applicant's arguments).
2. There is insufficient motivation to use the BIBAC vectors taught by Hamilton 1977 to transform host cells other than plant host cells. It is suggested that such an endeavor, whereby four references are combined to arrive at the instant invention, would require applying improper hindsight construction in the rejection (see for example the 7th and 8th paragraphs of page 12 of Applicant's arguments).

Applicant's arguments are not considered persuasive for the following reasons:

1. Applicant's contention appears to be that the secondary references do not teach the elements of the claims concerning agrobacterium-mediated transformation of yeast cells (such as *S. cerevisiae* or *K. Lactis*) and filamentous fungi such as (*Aspergillus*); it is noted that there is no

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indication that the vectors described in the Hamilton 1997 or Hamilton '744 references cannot be used in the claimed invention. In contrast to Applicant's assertion, the references do clearly teach the limitations of agrobacterium-mediated transformation of yeast cells and filamentous fungi. Bundock teaches the transformation of the yeast *S. cerevisiae* using an agrobacterium/binary vector (see the entire document, for example the Abstract and the paragraph bridging pages 3207 and 3208). Similarly, de Groot teaches the transformation of the filamentous fungi *Aspergillus* (see the entire document, for example the Abstract) using a binary agrobacterium-based vector system. These elements were clearly indicated in the previous Office Action (see pages 8 and 9). Therefore, the argument that these elements are not taught by the indicated references is erroneous.

2. Applicant argues that there is no motivation to combine the references to arrive at the instantly claimed invention, and that such a reconstruction from four separate references would require impermissible hindsight. The argument appears to have two main points: (a) that impermissible hindsight is used; (b) that the number of references influences the validity of the obviousness rejection. These issues are dealt with separately below.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, it is clear that the vectors to be used in the

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claimed methods were known at the time of the invention; this is because there are no arguments or evidence provided that the agrobacterium-based binary vectors taught by Hamilton 1997 and Hamilton '744 are not vectors that would be used in the claimed methods (i.e., the vectors taught by the references would unquestionably be used in the claimed methods). Thus, the inventive step in this instance is the use of these vectors to transform non-plant host cells, particularly yeast, filamentous fungi and mammalian cells. It is this step that must be obvious and taught by another reference that supplies sufficient motivation to combine the teachings.

The de Groot reference teaches the transformation of filamentous fungi with an agrobacterium-based binary vector, making it obvious to use any agrobacterium-based binary vector. This includes the BIBAC agrobacterium-based binary vector taught in the Hamilton references, absent any evidence to the contrary. The de Groot reference further teaches that the transformation of filamentous fungi with an agrobacterium-based binary vector has great benefit for improving transformation of filamentous fungi, which are attractive hosts for large-scale recombinant protein production (see for example the second and third paragraphs of page 839 of the reference as cited in the previous Office Action). This provides motivation to use a particularly efficient agrobacterium-based binary vector, such as the BIBAC vector taught by Hamilton 1997 and Hamilton '744 (which minimizes size and maximizes stability-see the paragraph bridging p.109-110), because the ordinary skilled artisan would recognize the benefits of improved transformation of filamentous fungi using agrobacterium-based binary vectors. Thus, there is indeed motivation to combine the de Groot and Hamilton 1997/ Hamilton '744 references.

The Bundock reference teaches the transformation of the yeast *S. cerevisiae* with an agrobacterium-based binary vector, making it obvious to use any agrobacterium-based binary vector. This includes the BIBAC agrobacterium-based binary vector taught in the Hamilton references, absent any evidence to the contrary. The Bundock reference further teaches that the use of agrobacterium-based binary vectors to transform *S. cerevisiae* can be used to study the interaction/influence of agrobacterium on recombination and as a powerful tool to perform genetic modification in species that are recalcitrant to transformation (see for example the first full paragraph on the right column of page 3212). This provides motivation to use a particularly efficient agrobacterium-based binary vector, such as the BIBAC vector taught by Hamilton 1997 and Hamilton '744 (which minimizes size and maximizes stability-see the paragraph bridging p.109-110), because the ordinary skilled artisan would recognize the benefits of agrobacterium-based transformation of *S. cerevisiae* as indicated in the Bundock reference. Thus there is indeed motivation to combine the Bundock and Hamilton 1997/ Hamilton '744 references.

In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Furthermore, it is brought to the attention that the ordinary skilled artisan need not combine all four references to arrive at any given invention. The references were indicated together because the claims read on multiple species (i.e., yeast cells, filamentous fungal cells, etc.), and these species were addressed collectively to avoid a repetitious rejection. Thus, it would be obvious to the ordinary skilled artisan to combine the

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teachings of the Hamilton 1997 and Hamilton '744 references separately with the de Groot and Bundock references to arrive at a given species claimed.

In conclusion, Applicant's arguments are not found convincing because, as set forth above, there is a significant level of obviousness to combine the teachings of Hamilton 1997, Hamilton '744, de Groot and Bundock to arrive at the instant invention. This is because the inventive step, the transformation of non-plant cells with an agrobacterium-based binary vector, has been performed before. Furthermore, there is substantial "two-way" motivation (meaning both references used have motivation to combine the references) to combine the references, wherein the Hamilton references make use of a vector that is minimized in size and maximized for stability, and the de Groot and Bundock references provide clear benefits for the transformation of non-plant cells with an agrobacterium-based binary vector. As a result, the rejection set forth in the previous Office Action is maintained.

Allowable Subject Matter

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson, Ph.D.
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JAMES KETTER
PRIMARY EXAMINER